Doc Code: AP.PRE.REQ

PTO/SB/33 (07-05)
Approved for use through xx/xx/200x. OMB 0651-00xx
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): 2609/68518-A/JPW/GJG/ALW

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

on December 22, 2006

Signature: Gary J. Gershik

Typed or printed name: Gary J. Gershik

Application Number	Filed
10/758,572	January 14, 2004

First Named Inventor: Sharon Cohen-Vered

Art Unit	Examiner
1653	A. Desai

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant/inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [X] attorney or agent of record. Registration number 39,992
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

Gary J. Gershik
Signature

Gary J. Gershik
Typed or printed name

212-278-0400
Telephone number

December 22, 2006
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

- [ ] *Total of _____ forms are submitted.

Docket No. 68518-A/JPW/GJG

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Sharon Cohen-Vered, et al.

Serial No.: 10/758,572 Art Unit: 1653

Filed : January 14, 2004 Examiner: A. Desai

For : PARENTERAL FORMULATIONS OF A PEPTIDE FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

1185 Avenue of the Americas
New York, New York 10036
December 22, 2006

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SIR:

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Pursuant to a July 12, 2005 Notice in the Official Gazette, applicants respectfully request that a panel of Examiners review the final rejection under 35 U.S.C. §103 of the above-identified application.

Upon receiving the September 22, 2006 Final Office Action, which did not address all of applicants' remarks in support of patentability, applicants scheduled an Examiner interview on November 22, 2006. However, after receiving and discussing with SPE Kathleen Kerz applicants' outline of topics for the interview, the Examiner requested cancellation of the interview and agreed to reconsider the propriety of the obviousness rejection if a formal response to the September 22, 2006 Final Office Action was filed. A response to the September 22, 2006 Final Office Action was filed on November 22, 2006. The December 12, 2006 Advisory Action, however, did not address all of applicants' remarks in support of patentability, but maintained the obviousness rejections of the claims.

Applicants are filing this Request in an effort to obtain consideration of their reasons in support of patentability, first presented in applicants' June 27, 2006 Amendment, which remain unaddressed and unopposed on this record. Applicants respectfully submit that a *prima facie* case of obviousness has not been established.

This Request is being filing concurrently with a Notice of Appeal in a separate paper.

The Rejections Under 35 U.S.C. §103

On pages 3-4, in Sections 5-8 of the September 22, 2006 Final Office Action, the Examiner maintained the rejections of the claims under 35 U.S.C. § 103.

Applicants' Reply

In response, Applicants respectfully submit that the obviousness rejections maintained in the September 22, 2006 Final Office Action are deficient in at least the following elements:

1. THE PRIOR ART FAILS TO IDENTIFY A SOLUBILITY PROBLEM WITH THE POLYPEPTIDE RECITED IN THE PENDING CLAIMS.

Applicants are claiming formulations of a specific peptide. The September 22, 2006 Final Office Action, to purportedly show existence of motivation, referred to paragraph [0088] of the Mozes application, presumably to the last sentence of the paragraph. This sentence, however, a) does not indicate that there is any solubility problem, and b) teaches that "derivatives and salts" can "modify . . . stability, solubility, etc.," if needed. A cyclodextrin as claimed by Applicants is neither "derivatives" nor "salts". Applicants, therefore, maintain that the need for a cyclodextrin (or of any solubility enhancer at all) is simply not taught or suggested by the Mozes application.

Thus, absent Applicants' disclosure of a solubility problem, there is nothing of record except hindsight motivating the combination of the peptide of Mozes with any solubility enhancer, much less the cyclodextrin of the Hora '856 patent. This is a fundamental deficiency of the obviousness rejection of record.

2. THE PRIOR ART FAILS TO TEACH SELECTION OF CYCLODEXTRINS FROM AMONG THE MULTITUDE OF SOLUBILITY ENHANCERS.

Cyclodextrins are not a common class of solubility enhancers. Cyclodextrins are expensive and have known problems, as explained on pages 14-15 of Applicants' July 27, 2006 Amendment. The September 22, 2006 Final Office Action did not dispute this.

The primary reference, Mozes, does not indicate there is any need to use cyclodextrins; nor does Hora '856 suggest using its cyclodextrin with the specific peptide claimed by applicants. In fact, Mozes teaches away in its paragraph [0088] from using expensive cyclodextrins by recommending that solubility and stability can be modified by making "derivatives and salts" of the peptide. A cyclodextrin as claimed by Applicants is neither "derivatives" nor "salts".

Nothing of record teaches the selection of Hora '856 and its combination with applicants' specific peptide. Nothing of record shows that cyclodextrins would have any advantage if used with applicants' specific peptide.

3. THE PRIOR ART FAILS TO PROVIDE AN EXPECTATION THAT THE COMBINATION OF CYCLODEXTRIN WITH THE SPECIFIC RECITED PEPTIDE WOULD IMPROVE SOLUBILITY OF THE RECITED PEPTIDE.

Whether any given solubility enhancer would be effective for a given peptide class cannot be predicted. The September 22, 2006 Final Office Action did not dispute this.

For example, applicants needed to test over 40 solubility enhancers to find several that could improve the solubility of the recited peptide. See, pages 23-31 of the subject application. Table 2, part A of Hora shows that cyclodextrins are not universally effective (human growth hormone was still "lazy").

Therefore, one of skill could not expect that the solubility of the specific recited peptide would be improved by cyclodextrins.

4. THE PRIOR ART FAILS TO PROVIDE AN EXPECTATION THAT THE COMBINATION OF CYCLODEXTRIN WITH THE SPECIFIC RECITED PEPTIDE WOULD RESULT IN A BIOLOGICALLY ACTIVE PHARMACEUTICAL COMPOSITION.

Even if a solubility enhancer improves the solubility of a peptide, one of skill is acutely aware that the resulting composition may not be biologically active. The September 22, 2006 Final Office Action did not dispute this.

See, for example, Applicants' results with PEG 400, which improved solubility but eliminated biological activity of the recited peptide (page 25, lines 8-12 of the subject application). See, also, Table 3 of Hora '856 showing that 2 of the three formulations with cyclodextrin had significantly reduced bioactivity (36% and 45% less!). Hora '856 also excluded a fourth formulation with insulin from its table 3 and acknowledged that its bioactivity was significantly different by excluding insulin from the sentence in its column 3, lines 61-62.

Clearly, therefore, the prior art did not provide the expectation of success necessary for a proper obviousness rejection.

Applicants note the September 22, 2006 Final Office Action relies on Stella et al. to assert that cyclodextrins "reduced toxicity,

and reduced membrane disruption ..." However, Stella et al. do not teach that a cyclodextrin always maintains bioactivity of the compound. More importantly, Stella et al. deal with small molecule drugs, and clearly cannot offer any teaching relevant to peptides, much less relevant to the claimed peptide.

Conclusion

In conclusion, Applicants respectfully maintain that the claimed invention is inventive over the prior art. Applicants also maintain that the obviousness rejections of record are fundamentally deficient for any one of the four reasons discussed above, which remain unaddressed and unopposed on this record. Accordingly, Applicants respectfully request that the rejections be reconsidered and withdrawn.

No fee is deemed necessary in connection with the filing of this Pre-Appeal Brief Request For Review. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

Gary J. Gershik

John P. White
Registration No. 28,678
Gary J. Gershik
Registration No. 39,992
Attorneys for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Gary J. Gershik 12/22/06

John P. White Date
Reg. No. 28,678
Gary J. Gershik
Reg. No. 39,992